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NORRIS, MCLAUGHLIN & MARCUS, PA
875 THIRD AVENUE
18TH FLOOR
NEW YORK, NY 10022

EXAMINER	
GUDIBANDE, SATYANARAYAN R	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,524	AZZAWI ET AL.	
	Examiner	Art Unit	
	SATYANARAYANA R. GUDIBANDE	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/6/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/16/06,7/6/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I (claims 1-7) and election of anti-human IgG antibody form the goat in the reply filed on 3/17/09 is acknowledged.

The traversal is on the ground(s) that:

1. Claim 8 (group II invention) expressly relates "an apparatus for performing the process according to claim 1". Applicants argue about the lack of unity established in the instant application by citing a section of the MPEP 1850(III) with emphasis on the subsection (B) that states: "In addition to an independent claim for a given process, an independent claim for an apparatus or means specifically designed for carrying out the said process", and further that "[T]he expression 'specially designed' does not imply that the apparatus or means could not be used for carrying out another process, nor that the process could not be carried out using an alternative apparatus or means" implying that the lack of unity established in the instant case was improper. Applicants further argue stating that "[t]he office has not shown that Subramanian US 5,244,816 is capable of performing the process according to claim 1 and therefore, that the apparatus of claim 8 is not specifically designed for carrying out the process of claim 1" (emphasis added by the office).

2. Applicants argue that office adopted the restriction practice applicable to US national phase application and not the practice of 'Unity of invention' applicable in international applications (chapters I and II). Applicants also bring to office's attention that EPO granted the parallel European application without any restriction.

3. Applicants further argue that office has not justified requirement for species election by not further explaining the 'mutually exclusive characteristics of different species of biomolecules" that would make these species of biomolecules distinct from one another. Applicants state that they are unclear 'what these mutually exclusive characteristics are?' Applicants' further states that the similarities between the different species of biomolecules enable them to be labeled by the instant method clearly outweigh any perceived differences.

This is not found persuasive because:

1. It should be noted that MPEP section 1850 (II) states that "Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims". Further the same section also defines further that, "[B]y dependent" it is meant a claim which contains all the features of one or more other claims and contains a reference, preferably at the beginning, to the other claim or claims and then states the additional features claimed (PCT Rule 6.4). The MPEP further states that "examiner should bear in mind that a claim may also contain a reference to another claim even if it is not a dependent claim as defined in PCT Rule 6.4. One example of this is a claim referring to a claim of a different category (for example, "Apparatus for carrying out the process of Claim 1 ...,". Hence in the instant case, the claim 8 although expressly relates by reciting 'the process according to claim 1', it is treated as an independent claim as per the afore stated MPEP guidelines, because, the instant claim 8 recites "[A]n apparatus for performing the process according to claim 1".

Further with regards to argument about the cited reference of Subramanian, applicants admit that the apparatus of claim 8 is not specifically designed for carrying out the process of claim 1.

2. With respect to applicant's argument that the International searching authority (ISA) did not find that the original claims as filed lacked unity of invention. This is not found persuasive because statements made by the International Searching Authority or International Preliminary Examining Authority are not controlling in applications filed in the national phase. The MPEP states "The examiner may adopt any portion or all of the report on patentability of the IPEA or ISA upon consideration in the national stage so long as it is consistent with U.S. practice. The first Office action on the merits should indicate the report on patentability of the IPEA or ISA has been considered by the examiner. The indication may be a mere acknowledgement." See MPEP 1893.03(e). Further, unity of invention is specifically authorized under 37 CFR 1.499. The MPEP states that "Examiners are reminded that unity of invention **>(not restriction practice pursuant to 37 CFR 1.141 -1.146)< is applicable in international applications (both Chapter I and II) **and** in national stage applications submitted under 35 U.S.C. 371." Thus, the mere fact that the International Searching Authority did not raise a lack of unity is not basis to prevent a lack of unity from being raised in the national application.

3. With respect to applicant's argument that they are unclear about the 'mutual exclusive characteristics of biomolecules' it should be noted that biomolecules such as protein, nucleic acids, carbohydrates, lipids, etc., are structurally and functionally distinct molecules and belongs to different classes. The polymeric biomolecules such as protein, nucleic acids and carbohydrates

are made of monomer subunits that are quite distinct from each other. The chemistry to label them is quite different from each other as they exhibit chemically distinct different functional groups amenable to such modifications.

Hence, the election/restriction requirement is still deemed proper and is therefore made FINAL.

Status of pending claims

Claims 1-8 are pending.

Claim 8 has been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/6/09.

Claims 1-7 are examined on the merit.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(a-d) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(a-d) as follows:

The foreign priority document submitted is not in English language. A translation of the same is required to grant the priority. The filing date of the priority document is not perfected

unless applicant has filed a certified priority document in the application (and an English language translation, if the document is not in English) (see 37 CFR 1.55(a)(3)).

Specification

1. The abstract of the disclosure is objected to because the abstract submitted is the first page of the WO 2005/064335 (i.e., the published PCT/EP04/12172). Hence, this application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. Correction is required. See MPEP § 608.01(b).

2. The disclosure is objected to because of the following informalities: The instant specification contains several drawings. However, the brief description of the several views of the drawing(s) has not been disclosed adequately to provide proper interpretation of the drawings.

Appropriate correction is required.

3. The specification of the instant application also lacks the required format for presentation as provided in 37 CFR 1.77(b). The instant specification does not conform to the guidelines with sections under different titles such as:

(b) Cross-reference to related applications,

(f) Background of the invention.

(1) Field of the invention.

(2) Description of related art including information disclosed under 37 CFR 1.97 and 1.98.

(g) Brief summary of the invention, etc.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Information Disclosure Statement (IDS)

The information disclosure statement filed 6/16/06 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Although, applicants state that the copies of the documents listed on IDS are in the national stage file, the copies of the foreign patents and non-patent literature documents are missing. The references for which copies are not available in the instant application file have not been considered and will be considered when the copies are placed in the file. Only the abstracts of five foreign patent documents have been placed in the file. The abstracts have been considered, however, copies of the documents (translation necessary if the document is in language other than English). Since the copies foreign patents have not been submitted in full in English language, the documents have been indicated as being not considered on the IDS.

Claim Objections

Claim 4 is objected to because of the following informalities: Claim recites "micromixer is a micromixer" in line 2. Instead the claim could be recited as "micromixer is a mixer" Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recite reactive groups as "wherein the free reactive groups are amino, thiol, alcohol, aldehyde/ketone and/or carboxylic acid groups". This is an improper Markush group. The proper way to recite the claim would be "wherein the free reactive group is selected from the group consisting of amino, thiol, alcohol, aldehyde, ketone and carboxylic acid groups."

Claim 3 recite biomolecules as "wherein the biomolecules are proteins, nucleic acids and/or saccharides.". This is an improper Markush group. The proper way to recite the claim would be "wherein the free reactive group is selected from the group consisting of proteins, nucleic acids and saccharides."

2. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is rejected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim as presented recite that the reaction mixture is pumped in circulation in the delay structure used and a micromixer is optionally being inserted into the circuit. The base claim as recited requires a micromixer in the process, however, the claim 7 as

presented recites that the insertion of micromixer is optional. Hence the claim 7 as recited improperly depend from the base claim for failing to further limit the subject matter of the base claim 1.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Spikmans, 2002, Rapid Communications in Mass Spectrometry, 16, 1377-1388.

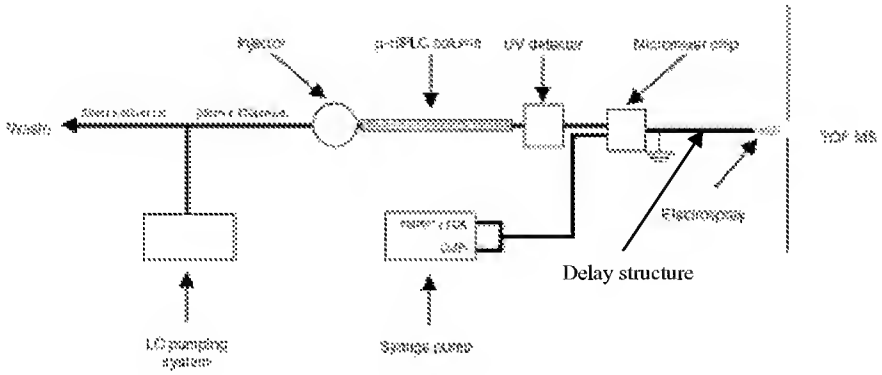
In the instant application, applicants claim a process for labeling biomolecules by reacting the reactive functional groups of biomolecules with a label. The process comprises, i) feeding solutions of both compounds in defined quantitative rates to a micromixer and ii) mixing intensively there. The process steps also comprises optional steps such as iii) feeding the reaction mixture into a delay structure, iv) retaining the (reaction mixture) there (in the delay structure) for a time predetermined by volume of the delay structure and flow rate of reaction mixture and v) terminating the reaction after a time predefined by the reaction condition.

Although, office has assigned Roman numerals to the different process steps, it is not required that the steps be performed in the same order as numbered or in any particular order, because the instant claim is drawn with the transitional phrase "comprising". The Roman numerals have been assigned by the office to help organize and craft the rejection properly.

As recited the invention claims a process of labeling biomolecules that bears free reactive groups with a label compound and forms a covalent bond. As presented the process requires feeding solutions of both compounds in defined quantitative flow rates to a micromixer and mixing intensively there. The other steps are being optional as recited.

Spikmans discloses a method of labeling amines, ketones and aldehydes (reads on instant claim 2) with a positively charged phosphonium compound for preinonization of the analytes (page 1378, column 2, paragraph 2). As shown in figure 1 on page 1379 (reproduced as shown

below), the sample (the compound of the instant invention) after undergoing separation by HPLC enters the micromixer chip (micromixer of the instant invention) via a UV detector.



The reagents for the derivatization (for labeling) are introduced into the second inlet of the micromixer chip by a dual syringe pump (page 1380, column 2, paragraph 1). Spikmans further discloses that all parameters of the reaction such as flow rates and concentrations can be defined separately for optimization of the reaction and thus help or promote product formation (page 1380, column 2, paragraph 2). This reads on the steps (i) of the instant claim 1. Spikmans also discloses that microchip layouts have been proposed for mixing, including turbulent mixing and serial and parallel lamination (page 1378, column 1, paragraph 3). Since the reaction occurs in 'seconds' compared to 30 minutes reaction 'on the bench', it inherently implies that the reagents introduced into the micromixer mixes intensively to form products and hence reads on the step (ii) of instant claim 1. Spikmans also discloses that the method of labeling can be used for labeling n-terminus of a peptide (page 1381, column 1) and this reads on the biomolecule of instant claim 1. The instant claim 1 is drawn to a process for labeling biomolecules, an intended use.

Spikmans also discloses that in a study to emulate on-chip band broadening, the total volume of the system (micromixer) with the chip was mimicked in a system without the chip using a 100-μm inner diameter capillary. This inherently implies that the channel in the micromixer has diameter ~100 μm. This reads on the instant claim 4.

Spikmans also discloses that the micromixer that is developed is based on parallel lamination (page 1378, column 2, paragraph 1). This reads on the instant claim 5.

The figure 3 of the Spikmans discloses a connecting structure, i.e., a tube or capillary tube (as pointed out by an arrow in the figure above) that connects the micromixer to the mass spectrometer. This connecting capillary tube corresponds to the delay structure of the instantly claimed process. This connecting structure is of predefined volume determined by its defined length and cross sectional diameter of the tubing. This reads on the instant claim 6.

The reference of Spikmans does not explicitly teach that their process is used for the labeling of proteins, nucleic acids and/or saccharides.

However, Spikmans discloses that the method of labeling small molecule amines can be used for labeling N-terminus of a peptide (page 1381, column 1) and this reads on the biomolecule of instant claim 1 and the polypeptide (protein) of claim 6. Where applicant claims a process of labeling a protein or an antibody (elected species) a characteristic not explicitly disclosed by the reference, a 102/103 rejection is proper according to MPEP 2112. MPEP 2112 states that "[W]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in

concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re* Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims".

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R Gudibande/
Examiner, Art Unit 1654